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(54) Title: DETECTING BACTERIA

(57) Abstract

There is disclosed a method and apparatus for detecting bacteria comprising detecting gas or vapour associated with the bacteria.

DETECTING BACTERIA

This invention relates to detecting bacteria.

Bacteria are identified in a variety of ways. Many have characteristic forms which can be seen under microscopic examination, but some are identified, when colonised on a growth medium, by a characteristic colour and in some cases this is confirmed by smell. Not all bacteria have any appreciable odour, but many have a characteristic associated gas or vapour.

The invention comprises a method for detecting bacteria comprising detecting gas or vapour associated with the metabolic activity of the bacteria.

The detection can be used for identification by differentiating the gas or vapour from that associated with other bacteria.

The method may comprise abstracting gas or vapour from a detection region and flowing the same over an array of sensors of which an electrical property varies according to exposure to gases or vapours and observing the response of the sensors.

The sensors may comprise semi-conducting polymers the resistance or impedance of which varies according to exposure to gases or vapours.

The response of the sensors may be compared against a library of responses to known bacteria, or the response may be input to a neural net trained against known bacteria.

The detection region may comprise an enclosed space above a Petri dish or like laboratory culture dish.

The array of sensors may first be purged using a purging gas.

The invention also comprises apparatus for detecting bacteria comprising detector means for detecting a gas or vapour associated with the bacteria.

Said detector means may comprise an array of sensors of which an electrical property varies according to exposure to gases or vapours. The sensors may comprise semi-conducting polymers the resistance or impedance of which varies according to exposure to gases or vapours.

The apparatus may comprise a store for a library of responses to known bacteria and comparison means operable automatically to compare a given response against the library. The apparatus may also comprise a neural net the input to which comprises the array of sensors and which is trained against known bacteria.

The apparatus may comprise a probe for sampling a detection region by abstracting gas or vapour from said region to be passed to said detector means. Said probe may comprise a cover for enclosing a Petri or like laboratory culture dish or an area of growth medium thereon.

Said probe may comprise a carrier gas feed and return and the apparatus may comprise a source of carrier gas.

Embodiments of apparatus and methods for detecting bacteria according to the invention will now be described with reference to the accompanying drawings, in which :

Figure 1 is a diagrammatic illustration of a first embodiment;

Figure 2 is a diagrammatic illustration of a second embodiment;

Figure 3 is a diagrammatic illustration of an arrangement for detecting bacteria on a culture dish;

Figure 4 is a diagrammatic illustration of an arrangement for detecting bacteria in a nutrient broth; and

Figure 5 is a cluster analysis of vapour associated with three species of bacteria.

The drawings illustrate methods and apparatus for detecting bacteria comprising detecting gas or vapour associated with the bacteria, and, further, methods for identifying bacteria by differentiating such gas or vapour from gas or vapour associated with other bacteria.

Figures 3 and 4 illustrate abstracting gas or vapour from a detection region 11 and flowing the same over an array 12 of sensors 13 of which an electrical property varies according to exposure to gases or vapours and observing the respons of th s nsors 13.

The sensors 13 comprise semi-conducting polymers the resistance or impedance of which varies according to exposure to gases or vapours.

An array 12 of twenty sensors has been employed to distinguish the vapours associated with the bacteria Straphylococcus aureus, Eschericia coli and Group A beta-haemolytic streptococci.

Eight epidermiologically unrelated patient isolates of each species were recovered from frozen storage. Each bacteria isolate was cultured overnight in nutrient broth 40 in a glass Duran bottle 42 with a GL-45 screw cap. After overnight incubation at 37°C the cap was changed for a cap 44 with inlet and outlet ports. After a period of equilibration at 37°C the headspace vapour above the broth 40 was analysed by pumping same across the 20 sensor array 12 at a flow rate of $\sim$ 150 ml min^{-1}.

The outputs of the sensors 13 were analysed by computing means 46 employing the non-linear cluster analysis mapping technique of Sammon (Sammon Jr., J.W., IEEE Trans. on computers, Vol. C-18, No. 5, May 1969, pp401-409). Figure 5 shows the r sults of this analysis, indicating that xc llent separation is achieved betwe n the clust rs 50,52,54 associat d with

straphylococcus aureus, Eschericia coli and Group A beta-haemolytic streptococci respectively.

Figure 1 illustrates comparing the response of the sensors 13 against a library 14 of responses to known bacteria. Figure 2 illustrates inputting the response to a neural net 15 trained against known bacteria.

Figure 3 illustrates a further sampling arrangement wherein the detection region 11 comprises an enclosed space above a Petri dish 16 or like laboratory culture dish. A probe 17 comprises a cover for enclosing an area of bacterial growth 18 on a growth medium 19 in the dish 16.

The probe 17 comprises a carrier gas feed 21 feeding a carrier gas such for example as purified air or nitrogen. Prior to taking gas or vapour from a sample in, say, a Petri dish, the array 12 of sensors 13 is first purged of any residual substances from a previous sensing operation by directing over the sensors 13 a stream of purging gas, which, in this instance, is the same as the carrier gas. The gas is supplied from a pressur bottle 22.

The sensors 13 can be selected for sensitivity to a broad spectrum of gases or vapours associated with bacteria and the apparatus may also be arranged to indicate concentration by measuring the level of response. A broader spectrum and a greater sensitivity will be obtained from a given array size by using a.c. technology as taught in EP-B-0 286 307 than by simply measuring d.c. resistance.

In addition to bacteria, the method may be applied to the detection of microfungi.

It may be important to specify the state of the microorganism when making an observation. Gases or vapours associated with growing bacteria or microfungi may well be different from gases or vapours associated with the same organism in growth-arrest stage or when it has been weakened or killed.

However, the library may contain data on the gases or vapours associated with microorganisms in all possible states, or the neural net trained to recognise them, so the apparatus may also identify the state as well as the microorganism.

CLAIMS

1. A method for detecting bacteria comprising detecting gas or vapour associated with the bacteria.

2. A method for identifying bacteria comprising detecting gas or vapour associated with the bacteria and differentiating such gas or vapour from gas or vapour associated with other bacteria.

3. A method according to claim 1 or claim 2, comprising abstracting gas or vapour from a detection region and flowing the same over an array of sensors of which an electrical property varies according to exposure to gases or vapours and observing the response of the sensors.

4. A method according to claim 3, in which the sensors comprised semi-conducting polymers the resistance or impedance of which varies according to exposure to gases or vapours.

5. A method according to claim 3 or claim 4, comprising the response of the sensors against a library of responses to known bacteria.

6. A method according to claim 3 or claim 4, comprising inputting the response to a neural net trained against known bacteria.

7. A method according to any one of claims 3 to 6, in which the detection region comprises an enclosed space above a Petri dish or like laboratory culture dish.

8. A method according to any one of claims 3 to 7, in which the array of sensors is first purged using a purging gas.

9. Apparatus for detecting bacteria comprising detector means for detecting a gas or vapour associated with the bacteria.

10. Apparatus according to claim 9, said detector means comprising an array of sensors of which an electrical property varies according to exposure to the gases or vapours.

11. Apparatus according to claim 10, in which the sensors comprise semi-conducting polymers the resistance or impedance of which varies according to exposure to gases or vapours.

12. Apparatus according to claim 10 or claim 11, comprising a store for a library of responses to known bacteria and comparison means operable automatically to compare a given response against the library.

13. Apparatus according to claim 10 or claim 11, comprising a neural net the input to which comprises the array of sensors and which is trained against known bacteria.

14. Apparatus according to any one of claims 9 to 13, comprising a probe for sampling a detection region by abstracting gas or vapour from said region to be passed to said detector means.

15. Apparatus according to claim 14, said probe comprising a cover for enclosing a Petri or like laboratory culture dish or an area of growth medium thereon.

16. Apparatus according to claim 15, said probe comprising a carrier gas feed and return.

17. Apparatus according to claim 16, comprising a source of carrier gas.

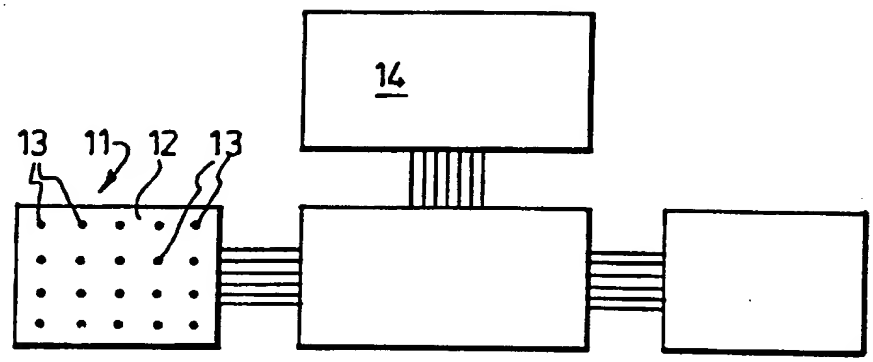

FIG.1

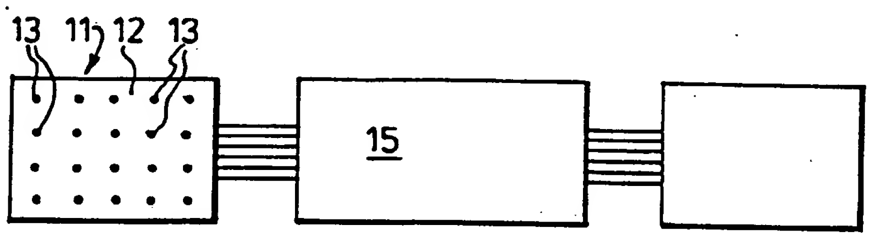

FIG.2

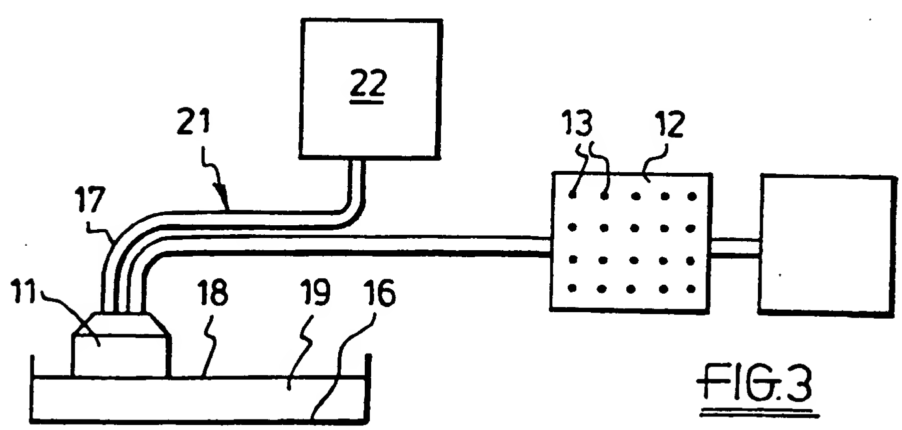

FIG.3

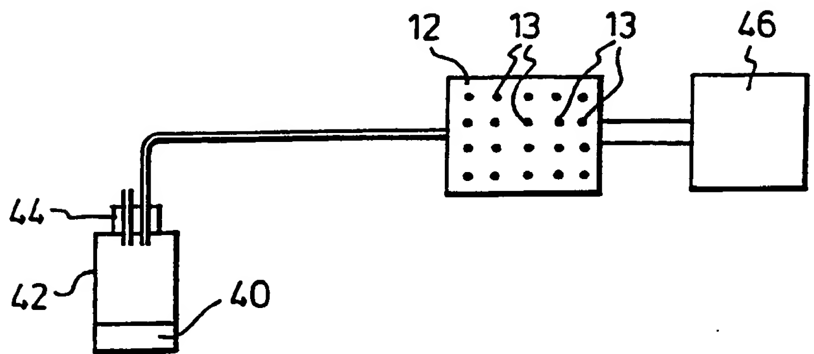

FIG.4

SAMMON MAPPING

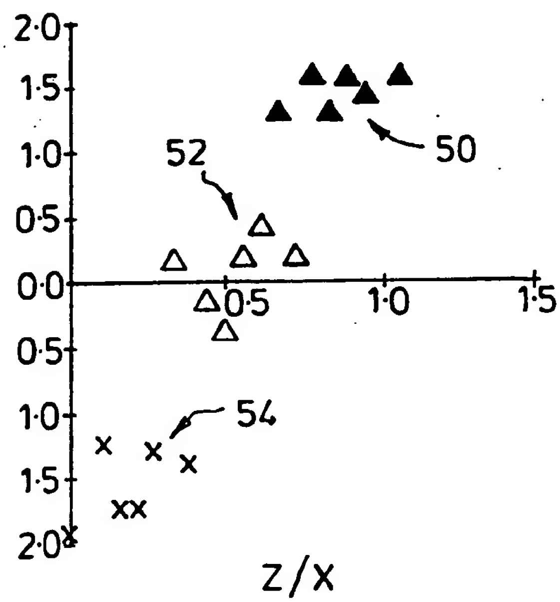

FIG.5

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 95/01347

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12Q1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 9 no. 283 (C-313) ,9 November 1985 & JP,A,60 130398 (KURITA KOGYO KK) 11 July 1985, see abstract	1
X	WO,A,94 04705 (MINI AGRICULTURE & FISHERIES ;STRACHAN NORVAL JAMES COLIN (GB); OG) 3 March 1994 see the whole document	1
X	EP,A,0 264 221 (BIOCONTROL SYSTEMS INC) 20 April 1988 see the whole document	1
X	EP,A,0 597 584 (BECTON DICKINSON CO) 18 May 1994 see the whole document	1

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 October 1995	16.10.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cartagena y Abella,P

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 95/01347

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB,A,2 176 901 (ATOMIC ENERGY AUTHORITY UK) 7 January 1987	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 95/01347

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9404705	03-03-94	AU-B-	4967493	15-03-94
		EP-A-	0656066	07-06-95
EP-A-0264221	20-04-88	US-A-	4868110	19-09-89
		AU-B-	7930187	14-04-88
		JP-A-	63152974	25-06-88
EP-A-0597584	18-05-94	US-A-	5310658	10-05-94
		AU-B-	4865893	21-04-94
		BR-A-	9304162	07-06-94
		CA-A-	2107289	10-04-94
		JP-A-	6197752	19-07-94
GB-A-2176901	07-01-87	NONE		